Brainstem auditory evoked potentials in late preterm infants at term-equivalent age

Chae-Ku Jo, Myo-Jing Kim

Department of Pediatrics, Dong-A University College of Medicine, Busan, Republic of Korea

E-mail: myojing@dau.ac.kr

Received: 19 June 2014, Revised: 4 November 2014, Accepted: 19 January 2015

SUMMARY: Jo CK, Kim MJ. Brainstem auditory evoked potentials in late preterm infants at term-equivalent age. Turk J Pediatr 2015; 57: 40-44.

To detect differences between late preterm and term infants in the brainstem auditory evoked response (BAER) variables that predispose to neurodevelopmental abnormalities, 36 late preterm infants and 87 term infants were recruited. Data collected with the click level at 70 dB nHL were used for analysis. The latencies of waves I (2.74±0.20 msec vs. 2.74±0.42 msec), III (5.55±0.33 msec vs. 5.53±0.45 msec) and V (7.55±0.34 msec vs. 7.59±0.44 msec), and the interpeak intervals for late preterm infants were similar to those for term infants. There were no significant differences between late preterm and term infants in amplitudes I (0.26±0.11 μ V vs. 0.24±0.10 μ V) and V (0.25±0.06 μ V vs. 0.28±0.11 μ V), and in the V/I amplitude ratio (1.10±0.47 vs. 1.23±0.46). There were no significant differences in the BAER variables between late preterm infants and term infants. Late preterm birth does not appear to have marked effects on neonatal BAER or development of the brainstem.

Key words: brainstem auditory evoked potentials, infant, premature.

The neurological maturation of the auditory system occurs in two phases. The first phase, peripheral maturation, takes place around the sixth month of fetal development. The second phase, the myelination of auditory pathways throughout the central nervous system, begins after birth and concludes within about 18 months^{1,2}.

Brainstem auditory evoked response (BAER), widely used as a tool to detect and diagnose peripheral and central auditory abnormalities in infants, provides a good objective estimate of the amount of peripheral auditory abnormality or hearing loss³⁻⁵.

Previous studies in preterm infants have shown an increase in BAER wave latencies and interpeak intervals when preterm infants reached term⁶⁻⁸. However, little has been reported about BAER in late preterm infants.

The aim of this study was to detect any differences between late preterm and term infants in BAER variables that predispose to neurodevelopment abnormalities.

Material and Methods

Subjects

The study was conducted retrospectively using medical records of infants admitted to the neonatal care unit at Dong-A University Hospital between March 2010 and February 2012. A total of 123 infants (36 late preterm infants and 87 term infants) were recruited. Thirty-six late preterm infants born at 34⁺⁰-36⁺⁶ weeks of gestational age constituted the study group. Eighty-seven term infants served as controls. All infants had no risk factors associated with hearing loss: no family history of hearing loss, birth weight over 1,500 g, no perinatal distress (average Apgar score was 9/10 at one/five minutes), no need for phototherapy due to hyperbilirubinemia, no ototoxic antibiotics treatments, no congenital infections and no facial anomalies. All infants were in a stable clinical condition at the time of BAER testing. Any infants who had a BAER threshold >20 dB normal hearing level (nHL) were excluded, because BAER components would be difficult to identify reliably in these infants.

The study was approved by the Institutional Review Board of the Dong-A Medical Center. Consent from the mother or the infant's legal representative was obtained at the time of hospital admission.

BAER recording and analysis

The recording of BAER was carried out at 37⁺⁰-42⁺⁶ weeks of postconceptional age (PCA) in infants born at 34⁺⁰-36⁺⁶ weeks of gestational age. In term infants, the recording of BAER was carried out within one month of birth. BAER was recorded using a Nicolet Viking Select system (Nicolet Biomedical Instrument Co., Madison, WI, USA).

The subjects lay supine in a cot in a quiet room. The recording was started after the subjects, who had been sedated (chloral hydrate 50 mg/kg/dose, administered orally), had fallen asleep. Three electrodes were placed on the middle forehead (positive), the ipsilateral earlobe (negative) and the contralateral earlobe (ground). Skin-to-electrode contact impedances were maintained at $<2 k\Omega$. The acoustic stimuli were rarefaction clicks of 100 μ s. BAER was recorded with clicks at a repetition rate of 11.3/s and 70 dB nHL. All noise to the contralateral ear was blocked. The brain responses to the click were amplified and filtered at 150-3000 Hz. Each run included the averaged brain responses to 500-1500 clicks. The intensity of the 11.3/s clicks was started at 90 dB nHL. If the main BAER waves could be clearly identified in the recording, the intensity of the clicks was decreased to 20 dB nHL and then decreased or increased by 10-20 dB steps until no clear and reproducible wave V was identifiable in the recording. The data collected with the click at 70 dB nHL were used for analysis.

Data analysis

The latency and amplitude of each BAER main component (waves I, III, V) were measured in the recording at 70 dB nHL. Interpeak intervals (I-V, I-III, III-V and III-V/I-III) and the V/I amplitude ratios were also calculated. All statistical values are shown as average±standard deviation. SPSS 19.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for the analysis. Two-tailed tests were used for all statistical tests, and the data were considered to have

statistical significance when the P value was less than 0.05. To compare the frequency and proportion of categorical variables, a chisquare test or Fisher's exact test was used. To analyze differences in the average between two independent groups, Student's t-test was used. All variables with a P value <0.05 were entered into a multivariate logistic regression analysis to identify risk factors affecting the BAER results.

Results

Clinical characteristics of the study subjects

In all, 36 late preterm infants and 87 term infants were recruited. There were 68 boys and 55 girls. Table I presents a comparison of demographic variables between late preterm and term infants.

Gestational age $(35^{+4}\pm1.0 \text{ weeks vs. } 38^{+5}\pm1.2 \text{ weeks, late preterm vs. term infants)}$ was significantly younger and birth weight $(2,361.9\pm559.4 \text{ g vs. } 3,113.1\pm536.2 \text{ g, late preterm vs. term infants)}$ significantly lower in late preterm infants (P<0.01).

There were no significant differences in sex, Apgar score and incidence of intrauterine growth retardation.

BAER recording in both groups was conducted within one month of term gestation. However, the PCA at BAER recording time in late preterm infants was slightly lower than that in term infants $(38^{+6}\pm1.9 \text{ weeks vs. } 41^{+2}\pm2.3 \text{ weeks})$ (P<0.01).

Comparison of BAER variables between late preterm and term infants

The BAER data obtained in the two groups of infants are presented in Tables II and III. The wave I $(2.74\pm0.20~\text{msec}~\text{vs.}~2.74\pm0.42~\text{msec})$, III $(5.55\pm0.33~\text{msec}~\text{vs.}~5.53\pm0.45~\text{msec})$ and V $(7.55\pm0.34~\text{msec}~\text{vs.}~7.59\pm0.44~\text{msec})$ latencies were similar in late preterm and term infants. The I-III $(2.77\pm0.31~\text{msec}~\text{vs.}~2.80\pm0.31~\text{msec})$, III-V $(2.03\pm0.29~\text{msec}~\text{vs.}~2.06\pm0.28~\text{msec})$ and I-V $(4.80\pm0.34~\text{msec}~\text{vs.}~4.85\pm0.35~\text{msec})$ interpeak intervals, and the III-V/I-III ratio $(0.74\pm0.14~\text{vs.}~0.75\pm0.13)$ were also similar for the two groups (late preterm vs. term infants).

There were no significant differences found when amplitudes I $(0.26\pm0.11~\mu V~vs.$

Table I.	Clinical	Characteristics	of the	Study	Patients
Table 1.	Cillincal	Characteristics	or the	Study	1 attents

Characteristics	Late preterm, n=36	Term, n=87	P
GA, weeks*	35+4±1.0	38+5±1.2	<0.01
Bwt, g*	$2.361.9 \pm 559.4$	$3,113.1 \pm 536.2$	< 0.01
Male, n (%)	20 (55.6)	48 (55.2)	1.00
IUGR, n (%)	6 (16.7)	7 (8.0)	0.30
AS1	7.0 ± 2.3	6.7 ± 3.0	0.63
AS5	8.5 ± 2.7	7.9 ± 3.2	0.35
PCA, weeks*	$38^{+6} \pm 1.9$	$41^{+2}\pm2.3$	< 0.01

n, number; GA, gestational age; Bwt, birth weight; IUGR, intrauterine growth retardation; AS1, Apgar score at one minute; AS5, Apgar score at five minutes; PCA, postconceptional age

 $0.24\pm0.10~\mu V$) and V $(0.25\pm0.06~\mu V$ vs. $0.28\pm0.11~\mu V$) and the V/I $(1.10\pm0.47~vs.$ $1.23\pm0.46)$ amplitude ratio were compared between late preterm and term infants. In the univariate analysis, gestational age, birth weight and PCA at BAER recording time were different in the two groups (P<0.05). To identify the risk factors affecting the BAER results, we conducted a multivariate logistic regression analysis with these variables. In this analysis, the BAER results in late preterm were not significantly different from those in term infants.

Discussion

Brainstem auditory evoked response (BAER) assesses the transmission of sound from the middle ear through the cochlea, auditory nerve and brainstem⁹. BAER responses are a function of the acoustic properties of the chosen stimulus and the method of presentation; they are not affected by sleep state, sedatives, anesthetics or anticonvulsants¹⁰. Thus, BAER

has been widely used to assess functional development of the auditory brainstem or, in a more general sense, the central nervous system in infants^{11,12}. Useful measurements for BAER during monitoring include the latencies of waves I, III and V. The I-III, III-V and I-V interpeak intervals as well as the V/I amplitude ratio are also useful¹³⁻¹⁵.

Many authors have reported that BAER results are influenced by the auditory maturation process and that their characteristics differ between premature and full-term babies^{8,16}. Previous studies demonstrated that the latency of waves I, III and V diminished as gestational age increased^{1,6}. To detect any differences between late preterm and term infants in BAER variables that predispose to neurodevelopmental abnormalities, this study observed differences in the functional behavior of the auditory system through a BAER analysis in late preterm and full-term infants comparing the absolute latencies of peaks I, III and V and the interpeak intervals I-III, III-V and I-V, as well as the V/I amplitude ratio.

Table II. BAER Wave Latencies and Interpeak Intervals in Late Preterm Infants and Term Infants

BAER variables	Late preterm, n=36	Term, n=87	Adjusted OR	P
I (msec)	2.74±0.20	2.74 ± 0.42	0.934	0.98
III (msec)	5.55 ± 0.33	5.53 ± 0.45	1.186	0.82
V (msec)	7.55 ± 0.34	7.59 ± 0.44	1.540	0.58
I-III (msec)	2.77 ± 0.31	2.80 ± 0.31	1.305	0.74
III-V (msec)	2.03 ± 0.29	2.06 ± 0.28	1.397	0.64
I-V (msec)	4.80 ± 0.34	4.85 ± 0.35	1.303	0.50
III-V/I-III	0.74 ± 0.14	0.75 ± 0.13	0.843	0.91

n, number; OR, odds ratio

BAER variables	Late preterm, n=33	Term, n=66	Adjusted OR	P
Ι (μV)	0.26±0.11	0.24±0.10	0.914	0.45
V (μV)	0.25 ± 0.06	0.28 ± 0.11	0.933	0.14
V/I	1.10 ± 0.47	1.23 ± 0.46	0.865	0.18

Table III. BAER Wave Amplitudes and Amplitude Ratios in Late Preterm Infants and Term Infants

n, number; OR, odds ratio

In the present study, there were no significant increases in any BAER latencies or interpeak intervals or the V/I amplitude ratio in late preterm infants when these measurements were compared with those of infants born at term. Our results indicate that brainstem auditory function in late preterm infants is similar to that in infants born at term.

The I-III interval reflects the expression of the functional activity of both the intracranial portion of cranial nerve VIII (wave II) and the lower brainstem^{15,17,18}. In the present study, the I-III interval in late preterm infants was similar to that of those born at term, reflecting a basically normal efficacy of synaptic transmission in late preterm infants.

The III-V interval reflects the functional status of the more central regions of the auditory brainstem^{13,15}. The III-V interval was also similar between the two groups in this study. Thus, there was no appreciable abnormality in the more central regions of the auditory brainstem in the late preterm infants.

The amplitude of a BAER component is typically measured from the peak of the component to its succeeding trough. The amplitude depends on the amount of neural activity generated, the degree of synchronization among the neural elements activated, or both 13,17,18. V/I amplitude ratio is the amplitude of wave V divided by the amplitude of wave I. The rationale for this amplitude ratio is, like that for the wave I-V delay, the assumption of desynchronization^{13,15}. In this study, the amplitudes and V/I amplitude ratio were similar between the two groups. There were no differences in neural activity or degree of synchronization in late preterm infants compared with term infants.

In conclusion, there were no significant differences in the BAER variables between late preterm infants and those born at term. Thus, the functional development of the auditory brainstem in late preterm infants is basically similar to that in term infants. Late preterm birth does not appear to have any marked effects on neonatal BAER or development of the brainstem. Based on the findings of this study, we suggest that the normal data and BAER criteria obtained from term infants can generally be used for late preterm infants when applying BAER as a tool for audiological evaluation. However, this retrospective study has some limitations. It did not include a comparison of the rate-dependent changes between the two groups. In addition, the number of subjects was relatively small. Therefore, further studies including rate-dependent changes and a larger number of subjects are needed to support our conclusion.

Acknowledgment

This work was supported by the Dong-A University research fund.

REFERENCES

- Sleifer P, da Costa SS, Cóser PL, Goldani MZ, Dornelles C, Weiss K. Auditory brainstem response in premature and full-term children. Int J Pediatr Otorhinolaryngol 2007; 71: 1449-1456.
- Rance G, Tomlin D. Maturation of auditory steady-state responses in normal babies. Ear Hear 2006; 27: 20-29.
- Jiang ZD, Brosi DM, Wu YY, Wilkinson AR. Relative maturation of peripheral and central regions of the human brainstem from preterm to term and the influence of preterm birth. Pediatr Res 2009; 65: 657-662.
- 4. Jiang ZD, Wilkinson AR. Normal brainstem responses in moderately preterm infants. Acta Paediatr 2008; 97: 1366-1369
- Yin R, Wilkinson AR, Chen C, Brosi DM, Jiang ZD. No close correlation between brainstem auditory function and peripheral auditory threshold in preterm infants at term age. Clin Neurophysiol 2008; 119: 791-795.
- Pasman JW, Rotteveel JJ, de Graaf R, Stegeman DF, Visco YM. The effect of preterm birth on brainstem, middle latency and cortical auditory evoked responses (BMC AERs). Early Hum Dev 1992; 31: 113-129.

- 8. Pasman JW, Rotteveel JJ, de Graaf R, Maassen B, Vicso YM. The effects of early and late preterm birth on brainstem and middle-latency auditory evoked responses in children with normal neurodevelopment. J Clin Neurophysiol 1996; 13: 234-241.
- 9. Jiang ZD, Brosi DM, Wilkinson AR. Auditory neural responses to click stimuli of different rates in the brainstem of very preterm babies at term. Pediatr Res 2002; 51: 454-459.
- deRegnier RA. Neurophysiologic evaluation of brain function in extremely premature newborn infants. Semin Perinatol 2008; 32: 2-10.
- Wilkinson AR, Jiang ZD. Brainstem auditory evoked response in neonatal neurology. Semin Fetal Neonatal Med 2006; 11: 444-451.
- 12. Jiang ZD, Brosi DM, Wang J, Wilkinson AR. Brainstem auditory-evoked responses to different rates of clicks in small-for-gestational age preterm infants at term. Acta Paediatr 2004; 93: 76-81.
- 13. Jiang ZD, Yin R, Shao XM, Wilkinson AR. Brain-stem auditory impairment during the neonatal period in term infants after asphyxia: dynamic changes in brain-stem auditory evoked response to clicks of different rates. Clin Neurophysiol 2004; 115: 1605-1615.

- 14. Don M, Kwong B. Auditory brainstem response: differential diagnosis. In: Katz J (ed). Handbook of Clinical Audiology (5th ed). Philadelphia: Lippincott, Williams and Wilkins; 2002: 274-297.
- Choi HJ, Lee TH, Oh KW, Kim HM. Auditory brainstem response (ABR) results in NICU graduates. Korean J Pediatr 2006; 49: 1301-1307.
- Chadha S, Bais AS. Auditory brainstem responses in high risk and normal newborns. Indian J Pediatr 1997; 64: 777-784.
- 17. Guilhoto LM, Quintal VS, da Costa MT. Brainstem auditory evoked response in normal term neonates. Arq Neuropsiquiatr 2003; 61: 906-908.
- 18. Jiang ZD, Brosi DM, Wilkinson AR. Brain-stem auditory function in very preterm infants with chronic lung disease: delayed neural conduction. Clin Neurophysiol 2006; 117: 1551-1559.
- Jiang ZD, Wilkinson AR. Brainstem auditory evoked response at term in preterm infants after perinatal hypoxia-ischaemia. Acta Paediatr 2006; 95: 1400-1404.